

GRADE Profile: What to Use in Second-line

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Date: 2009-08-21

Question: Should Lamivudine (3TC) be maintained in second-line antiretroviral regimens for patients failing first line therapy?

Settings:

Bibliography: Fox Z, Dragsted U, Gerstoft J, et al. A randomized trial to evaluate continuation versus discontinuation of lamivudine in individuals failing a lamivudine-containing regimen: the COLATE trial. *Antiviral Therapy* 2006;11(6):761-770.

Quality assessment							Summary of findings				Quality	Importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	No of patients		Effect			
							Maintaining 3TC in 2 nd line	No 3TC in 2 nd line (control)	Relative (95% CI)	Absolute		
Mortality - not measured¹												
0	-	-	-	-	-				-	-		CRITICAL
Progression of Disease - not measured												
0	-	-	-	-	-				-	-		CRITICAL
Severe adverse events (follow-up 48 weeks)												
1	randomised trials	no serious limitations ³	no serious inconsistency	serious ⁴	serious ⁵	none	-	-		Not estimable ²	⊕⊕○○ LOW	CRITICAL
Adherence/tolerability/retention - not reported												
0	-	-	-	-	-				-	-		CRITICAL
Virologic response (follow-up 48 weeks; measured as: mean reduction from baseline log₁₀ copies/ml of HIV RNA; Better indicated by higher values)												
1	randomised trials	no serious limitations	no serious inconsistency	serious ⁴	serious ⁵	none	28 ⁶	27	-	MD 0.4 lower (0.87 lower to 0.07 higher)	⊕⊕○○ LOW	IMPORTANT
Proportion achieving VL <50 copies/ml (follow-up 48 weeks)												
1	randomised trials	no serious limitations ²	no serious inconsistency	serious ⁴	serious ⁵	none	38/65 (58.5%)	30/66 (45.5%)	RR 1.29 (0.92 to 1.80)	132 more per 1000 (from 36 fewer to 364 more)	⊕⊕○○ LOW	IMPORTANT
Immunologic response (follow-up 48 weeks; measured as: median increase in CD4 from baseline⁷; Better indicated by higher values)												
1	randomised trials	no serious limitations	no serious inconsistency	serious ⁴	serious ⁵	none	65	66	-	median increase 11	⊕⊕○○ LOW	IMPORTANT

¹ Table 1 reports 1 death in Off3TC arm among patients who initiated treatment but discontinued

² Numbers provided are non-fatal clinical adverse events per arm/total adverse events (among 49 participants). Further information not provided. No difference in adverse events between arms; 43/94 (45.7%) events in On3TC arm and 51/94 (54.3%) events in Off3TC arm (p=0.25).

³ Open-label study; not downgraded for this. Partial funding from Industry in early phases of trial, also not downgraded for this (low risk of bias since study drug not favoured significantly by results).

⁴ Clinician optimized regimen; patients not from resource limited setting (study population from 12 European countries).

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⁵ Few events or low number of patients

⁶ Numbers represent Strata A, a priori sub-group of patients with only 1 prior 3TC containing regimen (n=55). Similar results for Strata B, those with more than 1 prior regimen (n=76). The mean reductions from baseline in HIV RNA in overall groups were 1.4 log₁₀ copies/ml (95% CI 1.1-1.6) in On3TC group and 1.5 (95% CI 1.2-1.7) in Off3TC group.

⁷ No SD or 95% CI available from study (IQR provided); unable to report mean difference between groups although median difference reported as not significant (+87 in On3TC compared to 76 in Off3TC group, p=0.41).